

### Amendments to the Drawings

Please replace the existing Figures 2 through 5 with the attached replacement sheets and an annotated sheet showing changes to Figures 2 through 5. In Figure 2 previously omitted reference characters 30, 34 and 38 have been added. In Figure 3 previously omitted reference terms directed towards the sample loading array, channel, subarray and microarray have been added. In Figure 4 previously omitted reference characters 10, 15, 18, 19, 40, 42 and 44 have been added. In Figure 5 previously omitted reference character 50 have been added.

Attachment: Replacement sheets  
Annotated Sheets Showing Changes

### **Remarks/Arguments**

By a non-final Office Action dated March 29, 2005, the Examiner in charge of this case rejected the claims of this application on a variety of grounds. The disposition of the claims is as follows: Claims 1-18 are currently pending in the application; Claims 2-6 and 14-18 have been withdrawn from consideration as being drawn to a non-elected invention; Claims 1, 7-10 and 13 are rejected under 35 U.S.C. 102(b); and Claims 11-12 are rejected under 35 U.S.C. 103 (a). The applicants have responded by submitting the amendments and comments set forth hereinbelow. Based on this submission, reconsideration of the merits of this patent application is respectfully requested.

### **Election/Restrictions**

In the Action, the Examiner has made final the requirement for restriction. The Examiner asserts that the process as claimed can be practiced by hand or an automated system. Although applicants respectfully disagree with the Examiner for the reasons stated in the reply filed on February 4, 2005, applicants acknowledge the finality of the restriction and reserve the right to rejoin the non-elected claims or present Claims 2-6 and 14-18 in a divisional application once the elected claims are found allowable.

### **Drawings**

The Examiner has objected to the drawings under 37 CFR 1.83(a) and 37 CFR 1.84 (p)(5). Specifically, the Examiner asserts that the phrases "first open end on a first side" and "second open end on a second side" as recited in Claim 7 must be shown or the feature(s) canceled from the claim. In response, applicants have amended Claim 7 to remove the above-mentioned phrases for clarification purposes. No new matter has been added. Support for the clarifying amendments to Claim 7 can be found, for example, at page 5, paragraphs [0022-0023] and page 6, paragraphs [0025-0026] of the specification.

The Examiner also asserts that Figures 2 through 5 do not include the reference characters mentioned in the specification. In response, applicants have amended Figures 2 through 5 of the drawings to comply with 37 CFR §1.84. Specifically, applicants submit herewith replacement sheets and corresponding annotated sheets for Figures 2 through 5, showing that the reference characters have been included.

### **Claim Rejections – 35 USC § 102**

Next, Claims 1, 7-10 and 13 were rejected under 35 U.S.C. 102(b) as being anticipated by Fernwood et al. (US 5, 141,719). Specifically, the Examiner asserts that Fernwood teaches the claimed invention because it discloses a method for processing biological, biochemical or chemical samples by the use of microtiter plates. Applicants respectfully disagree.

Applicants submit that Fernwood discloses a method for simultaneously filtering multiple samples into a well. Fernwood, also discloses a multi-well filtration plate assembly for purification of multiple samples simultaneously such that the resultant filtrate is eluted into individual collection wells. (See col. 2, lines 5-25; and Examples 1 and 2). In contrast the present invention describes a method for loading samples on sub-arrays of a microarray to perform sample hybridization reactions.

Specifically, applicants submit that the preamble and the steps of independent method Claims 1 and 7 have been amended for further clarity to include the following elements not disclosed by Fernwood. The first element of the method of Claim 1 now indicates that the sample loading array is a planar member having a plurality of micro-channels. The samples are then loaded into the micro-channels, to which is attached a porous membrane. The second element of the method of Claim 1 has also been amended to clarify that the hybridizations are performed by contacting the sample loading array with the microarray, by placing the fluid on the membrane to permit the samples in micro-channels to flow into contact with the substrate on the microarray. Support for these amendments may be found throughout the specification, such as, for example, at pg. 2, [0005-0006]; pg. 3, [0008]; pg. 4, [0017-0019]; pg. 5, [0022-0023]; pg. 6, [0024-0025]; and pg. 7, [0031]. Thus, contrary to the findings of the Examiner, Fernwood simply does not devise a process for loading samples on a microarray to perform multiple hybridization reactions, simultaneously.

Claim 7 was also amended herein to include the clarifying amendments made to Claim 1 with respect to the planar sample loading array, its placement on the microarray, and the presence of the common substrate, all of which facilitate the hybridization reactions to occur. In addition to these novel elements, Claim 7 recites that different samples are deposited in a plurality of micro-channels and that the sample loading array is aligned in such a way with the different sub-arrays of the microarray to facilitate the hybridization reactions. In contrast, Fernwood only discloses that all of the wells contain the same sample, it does not disclose depositing different samples.

Furthermore, not only are the elements of the method steps different, the filtration device of Fernwood is also quite different from the hybridization chamber of the invention. Unlike the present invention, Fernwood's device does not have a planar sample loading array member with channels and a porous membrane attached to it. Fernwood's device does not include sub-arrays within the microarray. Another technical difference is that Fernwood has a plurality of wells into which the filtrate is collected, but it does not remotely refer to the presence of a substrate anywhere on its filtration device. However, as indicated above the present invention includes a substrate on the microarray for use in hybridization reactions or for coupling with a hydrophobic group-bearing phosphoramidite to build a hydrophobic barrier area. (See pg. 4, [0017]; and pg. 5, [0022-0023]). Also, worthy of mention here is that the microarray hybridization chamber of the invention is capable of safely holding very small (as low as 200 nanoliters) sample volumes to conduct hybridization reactions, which is not technically possible using Fernwood's filtration system. (See pg. 2, [0006]).

Therefore, in view of the foregoing reasons, applicants submit that the elements of the method and device of Fernwood are strikingly different than that of the claimed invention and as such do not anticipate the claimed invention.

#### **Claim Rejections – 35 USC § 103**

Also, Claims 11-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Fernwood et al. (US 5, 141,719) in view of Bell et al. (US 5,858,194). Specifically, the Examiner asserts that although Fernwood fails to teach wells divided by a hydrophobic barrier, Bell discloses a device comprising capillaries and corresponding receptacles divided by an inhibitor or a hydrophobic barrier. The Examiner also asserts that phosphoramidite chemistry used in the present invention to build a hydrophobic barrier is known in the art, so it would have been obvious for a skilled artisan to provide such a barrier between the subarrays to prevent cross-contamination. Applicants respectfully disagree.

As discussed herein above, Fernwood discloses a simple filtration system having elements significantly different from the microarray hybridization chamber for parallel loading of samples. Applicants submit that the disclosure of Bell does not cure the deficiencies of Fernwood and therefore, does not make obvious the claimed methods. There are several for this assertion. First, Bell discloses components (capillary, interface and holder) of an capillary electrophoresis system, used in sample purification and sample analysis. Second, Bell does not disclose planar sample loading arrays, microarrays with

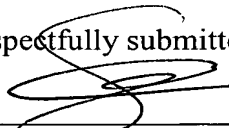
subarrays, substrates, or any of these elements for conducting hybridization reactions. Third, although, Bell briefly mentions using a hydrophobic barrier to reduce cross-contamination, the barrier is described as an “ink or a gap disposed between the adjacent receptacles” and not a hydrophobic barrier area comprising an activated substrate for coupling with a hydrophobic group-bearing phosphoramidite. (See Col. 3, lines 20-22). Thus, the fundamental scientific goals behind the methods of the invention (microarray hybridizations) and Fernwood and/or Bell (filtration and purification) is so different, that a skilled person would not even be inclined to try to combine their disclosures. Also, applicants believe that the skilled person would have no reasonable expectation that the methods used for sample filtration would apply equally well or at all to methods for performing simultaneous sample loading for hybridization reactions on a microarray. This was unprecedented in the art and it was not obvious before the work described in the present specification that this could be accomplished.

However, in an effort to obviate the rejection and avoid any need for further discussion on the topic, applicants have amended Claims 11 to clarify the difference between the barrier of Bell and the present invention. Support for the amendment may be found, for example at pg. 5, [0021]. As such, applicants submit that neither Fernwood or Bell, taken together or individually, make obvious claimed invention.

Accordingly, applicants respectfully request that in view of these claim amendments and comments, the rejection be respectfully reconsidered, withdrawn and that a timely Notice of Allowance be issued in this case.

A petition for a three months extension of time accompanies this response so the response will be deemed to have been timely filed. If any other fee is due or any other extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to the Deposit Account No. 17-0055.

Respectfully submitted,



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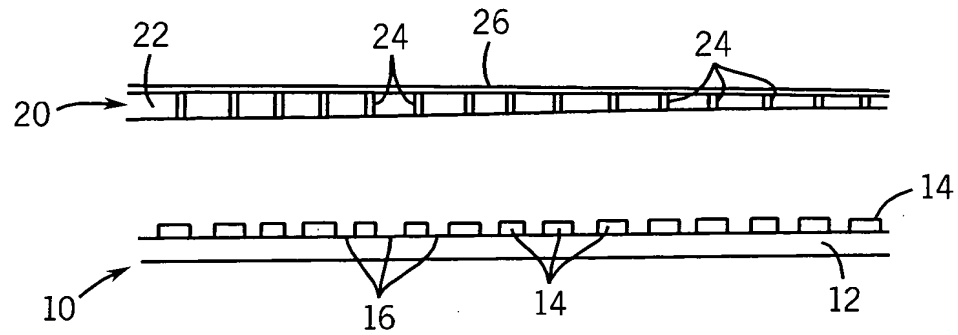


FIG. 1

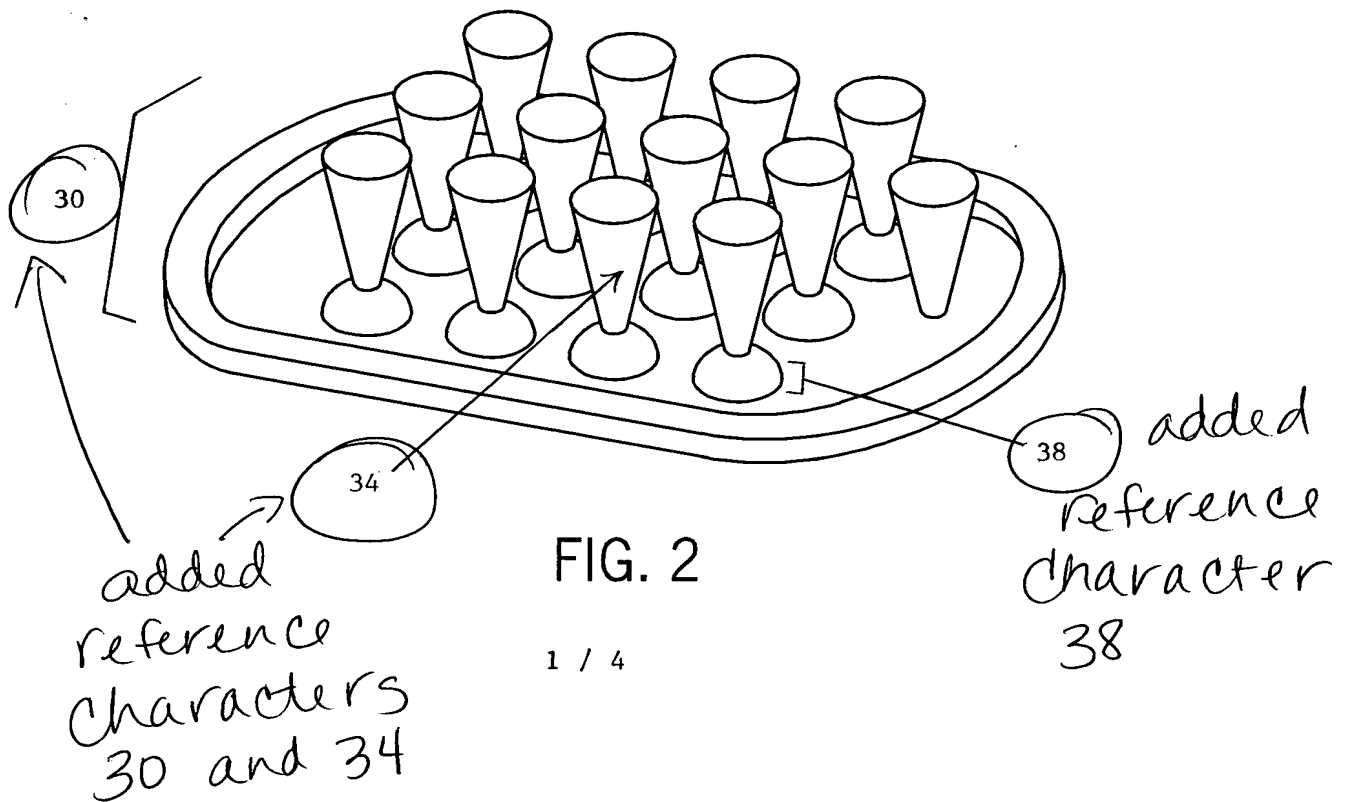
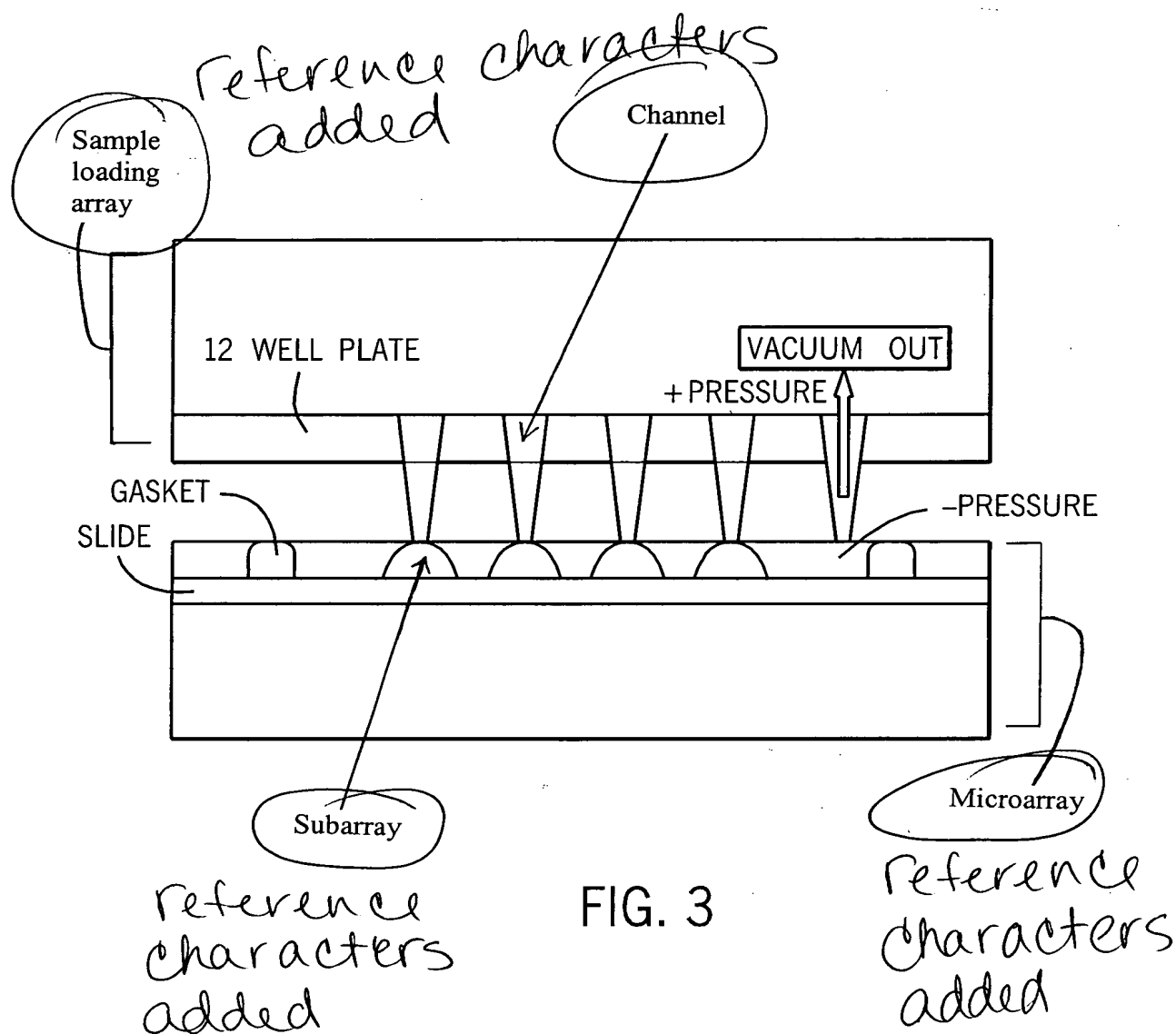
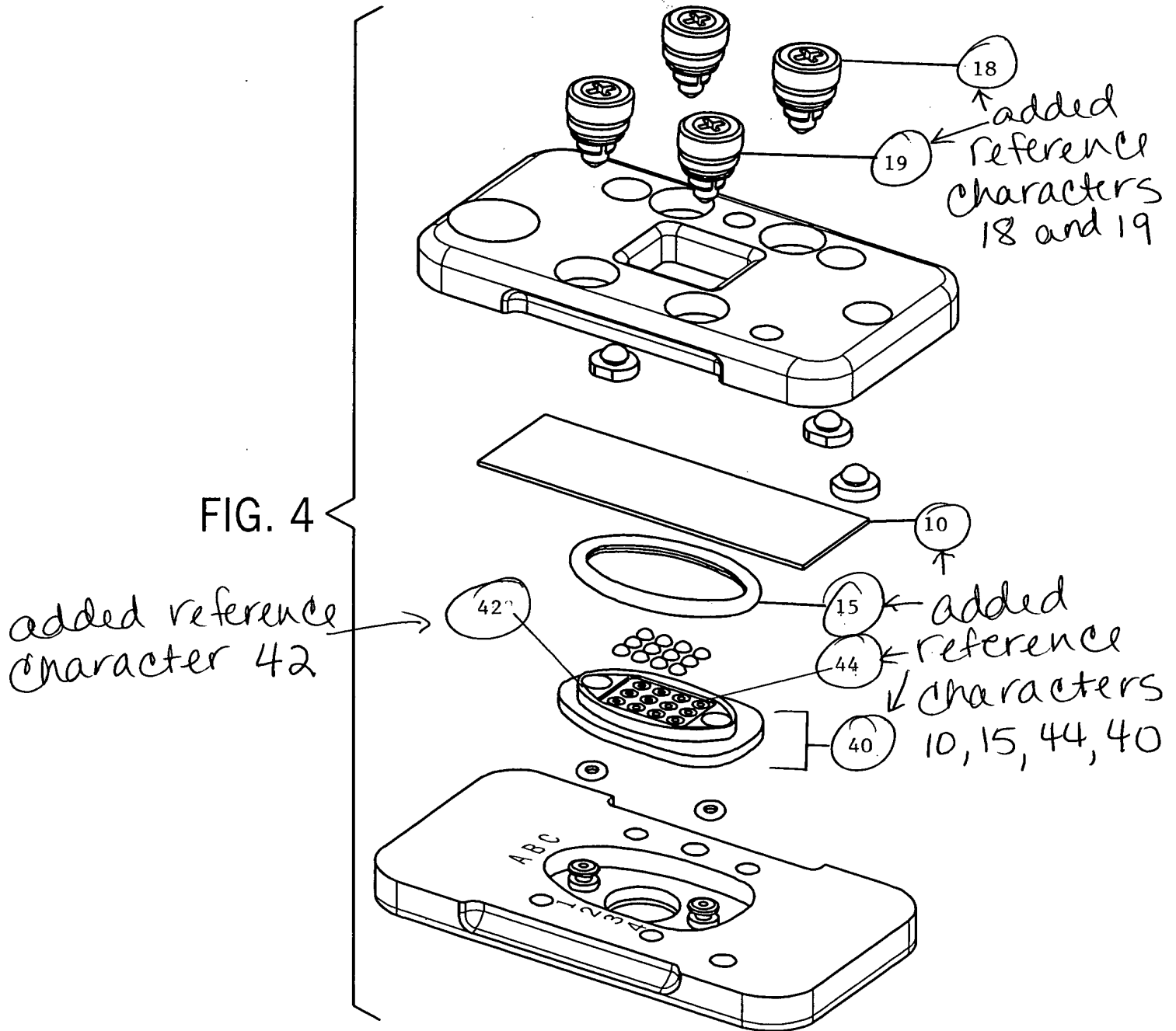


FIG. 2







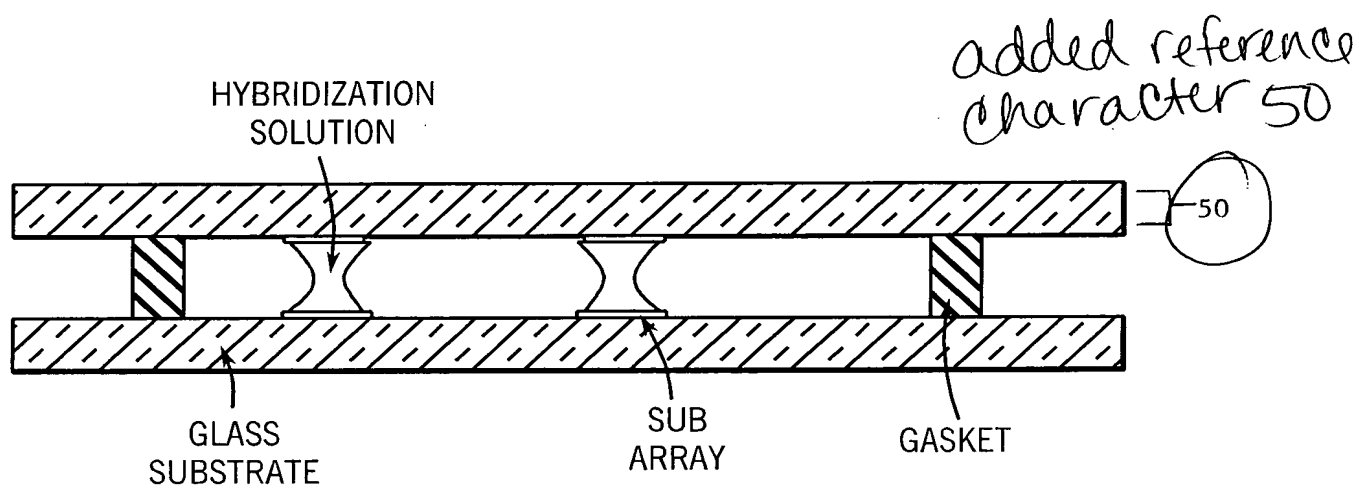


FIG. 5